# **EXECUTIVE SUMMARY**

## I. INTRODUCTION

On March 25, 2010, the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee will review and discuss the background information, the current performance standard, Medical Device Reporting information, recent information, including current literature regarding the risks to the general public from intentional exposure to ultraviolet radiation (UV) from use of ultraviolet lamps for tanning lamps.

There continues to be a growing body of literature showing association of skin cancer with use of tanning lamps and the committee will discuss this information and other information related to the association of UV and skin cancer (both melanoma and non-melanoma). The advisory committee will be asked to recommend whether changes to current device classification and/or current regulatory requirements applicable to UV lamps for tanning are needed.<sup>1</sup>

The following information will provide background to the Committee and the public and includes questions that the committee will be asked to answer in the public forum. The panel packet also contains several appendixes of materials including a recent report on the subject sponsored by the World Health Organization<sup>2</sup>

# II. BACKGROUND INFORMATION ON TANNING LAMPS AND BEDS

#### A. Tanning Lamp Usage in the United States

The practice of indoor tanning became widespread in Europe, particularly in the sundeprived northern countries, in the 1970s. The industry grew rapidly in the 1980s and 90s; today, according to the Indoor Tanning Association there are over 25,000 professional indoor tanning businesses in thousands of towns across America. Each year 30 million people—over 10 percent of the American public—visit an indoor tanning facility. The industry employs more than 160,000 Americans, mostly in small businesses. Its total economic impact exceeds \$5 billion annually.<sup>3</sup>

Tanning beds, which include multiple tanning lamps, are fairly commonly used by children and teenagers in the U.S. Cokkinides and his associates compared two surveys from 1998 (N-1196) and 2004 (N-1613) and found fairly consistent rates of usage in teenagers aged 11-

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<sup>&</sup>lt;sup>1</sup> http://www.fda.gov/AdvisoryCommittees/Calendar/ucm190824.htm

<sup>&</sup>lt;sup>2</sup> IARC Working Group on artificial ultraviolet light (UV) and skin cancer: the association of use of sun beds with cutaneous malignant melanoma and other skin cancers: A systematic review. 2006. Int J. Cancer 120:1116-1122.

<sup>&</sup>lt;sup>3</sup> http://www.theita.com/indoor/

18 of 10% and 11% in the two surveys.  $^4$  In serial surveys, Geller and coworkers found in a large survey (N-10,079 responders) that the overall use of tanning beds in 1999 was 9.5% The tanning lamp usage rate increased from 7% among 14-year-old girls to 16% by age 15, and more than doubled again by age 17 (35%; N = 244).  $^5$ 

There are also concerns that consumers may use tanning beds more than recommended. Hornung and his co-investigators in North Carolina conducted a survey of 453 participants who used 50 commercial tanning facilities during a state required inspection in 1994 and found that the recommended FDA limits were exceeded by 95% of patrons. <sup>6</sup>

## B. Tanning Lamps and History of FDA Regulations

Under the Federal Food, Drug, and Cosmetic Act, "devices" include those articles that, in part, are "intended to affect the structure of any function of the body of man or other animals" 21 U.S.C. 321(h). Ultraviolet lamps for tanning, including those used in tanning beds meet this definition because they are intended to introduce energy to the body, in order to change the structure or function of the body. The change in the structure of the body that is induced by UVB or UVA energy is the increase in melanocytes (pigment containing cells) that results in a tan. Complex dynamics play a role in these changes in individuals in response to repeated ultraviolet exposure according to Miller and her co-investigators. In 2008, Miller and co-workers from the FDA and the National Institutes of Health's Laboratory of Cell Biology published an article on the complex dynamics of pigmentation induction by repeated ultraviolet exposures that contribute to the formulation of a tan in the British Journal of Dermatology. <sup>7</sup>

The Code of Federal Regulations (CFR) classifies ultraviolet lamps for tanning and ultraviolet lamps for dermatologic disorders as class I and II medical devices respectively. The classification regulation for lamps for tanning is contained in 21 CFR 878.4635. Ultraviolet lamps for dermatologic disorders, also known as therapeutic UV devices, are classified in 21 CFR 878.4630. In 1990, the FDA classified tanning lamps as class I devices for which general controls are sufficient to assure safety and effectiveness. Though classified in Class I, tanning lamps remained subject to the premarket notification (510(k)) requirement until

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<sup>&</sup>lt;sup>4</sup> <u>Cokkinides V, Weinstock M, Lazovich D, Ward E, Thun M</u>. Indoor tanning use among adolescents in the US, 1998 to 2004. <u>Cancer.</u> 2009 Jan 1;115(1):190-8.

<sup>&</sup>lt;sup>5</sup> AC Geller, G Colditz, S Oliveria, K. Emmons, c. Jorgensen, GN Aweh, and AL Frazier. Use of Sunscreen, Sunburning Rates, and Tanning Bed Use Among More Than 10 000 US Children and Adolescents. Pediatrics, Jun 2002; 109: 1009 - 1014.

<sup>&</sup>lt;sup>6</sup> Hornung RL, Magee KH, Lee WJ, Hansen LA, Hsieh YC. Tanning facility use: are we exceeding Food and Drug Administration limits? J Am Acad Dermatol. 2003 Oct;49(4):655-61.

<sup>&</sup>lt;sup>7</sup> S.A. Miller, S.G. Coelho, B.Z. Zmudzka, H.F. Bushar, Y. Yamaguchi, V.J. Hearing, .Z. Beer Dynamics of pigmentation induction by repeated ultraviolet exposures: dose, dose interval and ultraviolet spectrum dependence. Briti Journ of Dermatol (2008) 159: 921–930.

December 7, 1994, when FDA amended the tanning lamp classification to exempt tanning lamps from the premarket notification procedures in subpart E of part 807.8

C. Current Code of Federal Regulations on Tanning Lamps

On July 25, 2001, 21 CFR 878.4635 was further modified to reflect that the exemption from premarket notification is "subject to the limitations in § 878.9." Section 878.9 outlines the circumstances under which a manufacturer would be required to submit a premarket notification for a device that is otherwise exempt from 510(k) requirements.

878.4630 Ultraviolet lamp for dermatologic disorders:

(a) Identification. An ultraviolet lamp for dermatologic disorders is a device (including a fixture) intended to provide ultraviolet radiation of the body to photoactivate a drug in the treatment of a dermatologic disorder if the labeling of the drug intended for use with the device bears adequate directions for the device's use with the drug.

21 CFR 878.4630 includes not only the UVA lamps used for treating psoriasis in combination with the drug psoralen (PUVA Therapy) but also both UVB and UVA phototherapeutic devices that are used for the treatment of other dermatological disease conditions such as vitiligo, atopic dermatitis (eczema) and leukoderma.

(b) Classification. Class II.

878.4635 Ultraviolet lamp for tanning.

- (a) Identification. An ultraviolet lamp for tanning is a device that is a lamp (including a fixture) intended to provide ultraviolet radiation to tan the skin. See § 1040.20 of this chapter.
- (b) Classification. Class I (general controls). The device is exempt from the premarket notification procedures in sub part E of part 807 of this chapter, subject to the limitations in § 878.9

In addition to being regulated as medical devices under 21 CFR 878.4635, ultraviolet tanning lamps are also regulated by FDA as radiation-emitting electronic products under 21 CFR 1040.20 - Sunlamp products and ultraviolet lamps intended for use in sunlamp products. (Sunlamp products performance standard). This regulation contains requirements for all ultraviolet tanning lamps, which include requirements regarding warning labels, limits on the ratio of UVC to UVB, protective eye wear, and timer systems.

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<sup>&</sup>lt;sup>8</sup> 59 Fed. Reg. 63010 (Dec. 7, 1994).

## D. Tanning Lamp Background

Originally many tanning beds used high pressure mercury vapor lamps as the source of UV for tanning and the majority of these beds used UVB as the tanning wavelength. Subsequently, a number of manufacturers developed fluorescent ultraviolet lamps which became the standard for most tanning beds with the initial lamps again being in the UVB range. Over time, as concerns for safety in commercial tanning facilities grew, a gradual move was made to develop combination UVB/UVA lamps with the thought that these would be potentially safer. Today many modern tanning beds use primarily UVA, but to increase the rate of tanning some are made with a high percentage of UVA and a smaller percentage of UVB<sup>9</sup>

The typical tanning bed found in most commercial facilities is of the "clam shell design". This type of tanning bed has a top cover which can be lowered over the subject, thus the name "clam shell". The subject lies on an acrylic transparent bed. UV lamps are in the cover (as well as in the bed) thus providing total body exposure. According to the sunlamp standard these beds are required to have a timer with settings that limit the exposure to 624 J/m², weighted with the FDA 'CIELYTLE' action spectrum for erythema (sunburn). This dose is meant to represent 4 minimal erythema doses for a light-skinned (Type II) individual.

# III. UV RADIATION, TANNING BEDS/LAMPS AND RECENT PUBLIC HEALTH ACTIONS

#### A. UV Radiation

It is known that UV radiation can produce genetic mutations that can lead to skin cancer. Both the U.S. Department of Health and Human Services<sup>10</sup> and the World Health Organization have identified UV as a proven human carcinogen.<sup>11</sup> UV radiation is considered the main cause of nonmelanoma skin cancers (NMSC), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). These cancers strike more than a million people worldwide, and more than 250,000 Americans, respectively, each year. Many experts believe that UV radiation plays a key role in the induction of melanoma, the deadliest form of skin cancer, which kills more than 8,000 Americans each year. Most people are exposed to large amounts of UVA throughout their lifetime. UVA radiation accounts for up to 95 percent of the UV radiation reaching the Earth's surface. UVA radiation is less effective at producing DNA damage than UVB, but it is present with

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<sup>&</sup>lt;sup>9</sup> Oliver H., Ferguson J., Moseley H. Quantitative risk assessment of sunbeds: impact of new high power lamps. Brit J Derm 157: 350-356, 2007.

<sup>&</sup>lt;sup>10</sup> U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program. Report on carcinogens, 11th ed: Exposure to sunlamps or sunbeds.

<sup>&</sup>lt;sup>11</sup> IARC Working Group on artificial ultraviolet light (UV) and skin cancer: the association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. 2006. Int J. Cancer 120:1116-1122.

relatively equal intensity during all daylight hours throughout the year, and can penetrate clouds and glass.

Studies over the past two decades show that UVA damages skin cells called keratinocytes in the basal layer of the epidermis, where most skin cancers occur. (Basal and squamous cells are types of keratinocytes.) UVA contributes to and may even initiate the development of skin cancers. It also plays a major part in skin aging and wrinkling (photoaging).

UVA radiation has become the wavelength region of choice for tanning, due to the fact that it is not as likely to produce a sun burn. It is recognized that tanning, whether outdoors or in a salon, causes cumulative damage over time. Tanning beds/booths primarily emit UVA. For a frequent tanner (100 sessions/year at 4 MED/session), exposure to high-pressure sunlamps could result in UVA doses as much as 12 times that of the sun. <sup>12</sup> UVB, the chief cause of skin reddening and sunburn, tends to damage the skin in the more superficial epidermal layers. It plays a key role in the development of skin cancer and a contributory role in tanning and photoaging. <sup>13</sup>

Many currently used tanning beds emit some combinations of UVA and UVB wavelengths to produce a tan (93 to 99 percent UVA and 7 to 1 percent UVB). The prevalent bio-effect of UVA radiation is tanning while that of UVB radiation is erythema (sunburn). Both wavelength ranges contribute to the production of tan<sup>14</sup>

# B. Recent Actions Involving Tanning Bed Usage

The World Health Organization in 2003 published a report aimed at international governmental policy makers entitled: Artificial Tanning Beds: Risk and Guidance. According to the WHO, in general, sun beds predominantly emit UVA radiation, which is thought to be the least damaging of the UV radiation spectrum. Some machines have the ability to emit UV radiation 5X stronger than the midday sun in a country like Australia. <sup>15</sup> However in recent years, some sun beds have been manufactured that produce higher levels of UVB to mimic the solar spectrum and speed the tanning process. Despite the types of UV radiation used, overexposure to UV radiation from the sun and artificial sources is of considerable public health concern. UV radiation plays an important role in the development of skin cancer, cataracts, and other eye conditions, and suppresses the immune system. Cumulative UV radiation also results in premature skin aging. This WHO Report recommended to policy makers that based on an International Commission on Non-

14 http://www.livestrong.com/article/43123-uva-vs.-uvb-tanning-beds/

<sup>&</sup>lt;sup>12</sup> Miller S.A., Hamilton S.L., Wester U.G., Cyr W.H., An analysis of UVA emissions from sunlamps and the potential importance for melanoma. Photochem Photobiol 68 (1): 63-70, 1998.

http://www.skincancer.org/understanding-uva-and-uvb.html

<sup>&</sup>lt;sup>15</sup> Standards Australia/Standards New Zealand Committee. Australian/New Zealand standard for the installation, maintenance, and operation of solaria for cosmetic purposes (revision of AS 2635-1983). AS/NZA 2635:2002. Sydney: Standards Australia, 2002.

Ionizing Radiation Protection<sup>16</sup> that people should not use tanning beds that tanning beds not be used by anyone under the age of 18.<sup>17</sup>

As discussed below in more detail in the health risk section, there is growing evidence that excessive exposure to UV results in premature aging of the skin; can lead to cataract formation; and has been declared a Class I carcinogen by the IARC, with evidence suggestive of melanoma and other skin cancer formation with an association to usage before and during young adulthood.

As of October 2008, 28 U.S. states have passed some type of restriction on the use of tanning beds with 11 setting various penalties for either the promotion or the sale of tanning bed usage to minors. <sup>18</sup>

As part the Food and Drug Administration Amendments Act of 2007, Congress required FDA to make certain determinations regarding the effectiveness of warning labels for indoor tanning devices, to conduct consumer testing in making these determinations, and to report to Congress on these determinations.

In December 2008, FDA submitted this report to Congress, entitled, "Labeling Information on the Relationship between the Use of Indoor Tanning Devices and Development of Skin Cancer or Other Skin Damage." <sup>19</sup> This report explained that FDA is considering amending the sunlamp products performance standard to improve consumer safety by requiring a warning statement that more clearly and effectively conveys the risks posed by tanning lamps and by harmonizing performance requirements with the international standard of the International Electrotechnical Commission (IEC). The IEC standard (60335-2-27) for tanning beds contains many of the same elements that are in the current FDA performance standard for sunlamp products. However, there are some differences; for example: (1) the IEC standard contains a limit on the intensity that can be emitted by tanning beds; (2) the IEC standard has different limits and requirements for tanning beds meant to be used in the home; and (3) the IEC standard defines five different types of tanning beds, based on their emission spectra. In addition, the IEC standard provides guidance on how many tanning sessions should be received annually, based, in part, on research conducted at the FDA. This research showed that the number of sessions could be reduced from what is currently recommended in the FDA 1986 guidance [http://www.fda.gov/downloads/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/HomeBusinessandEntertainme

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<sup>&</sup>lt;sup>16</sup> International Commission on Non-Ionizing Radiation Protection (ICNIRP). Health issues of ultraviolet tanning appliances used for cosmetic purposes. *Health Phys* 2003;84(1):119-27.

<sup>&</sup>lt;sup>17</sup> World Health Organization. Artificial Tanning Beds: Risk and Guidance. 2003 Available at: http://www.who.int/uv/publications/sunbedpubl/en/

<sup>18</sup> http://www.cdc.gov/PCD/issues/2008/oct/07 0194.htm

<sup>&</sup>lt;sup>19</sup> http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeand ModernizationActMDUFMA/ucm109288.htm.

nt/UCM192707.pdf]. This reduction in the number of sessions could result in a reduction of the cumulative dose by a factor of 2 to 3 below what is currently recommended. FDA also conducts educational outreach efforts to better inform consumers about the risks of indoor tanning. FDA most recently updated its consumer information regarding the potential serious health risks from the use of tanning beds on November 30, 2009. 21

On November 10, 2009, the Howard County, Maryland Board of Health voted to approve proposed regulations to ban individuals under the age of 18 from using indoor tanning beds. The vote came after a large public hearing held at the health department. Howard County becomes the first jurisdiction in the country to provide comprehensive protection for children against the dangers of indoor tanning. <sup>22</sup>

Representatives Carolyn Maloney (D- NY) and Charlie Dent (R-PA) have introduced, a bill entitled, The Tanning Bed Cancer Control: HR Act (H.R. 4520). On January 26, 2010, this bill was referred to the House Committee on Energy and Commerce for consideration.<sup>23</sup> <sup>24</sup>

On January 27, 2010 The Federal Trade Commission (FTC) charged the Indoor Tanning Association (ITA) with making false health and safety claims about indoor tanning. According to the FTC: indoor tanning; increases the risk of squamous cell and melanoma skin cancers contrary to the ITA's claims. The association has agreed to a settlement that bars it from any further deception. The FTC has also updated consumer information on the risks of tanning beds.

C. Professional Society Statements on Tanning Bed Usage

Two prominent medical specialty associations in the U.S. have provided recent statements on the position dangers of tanning:

American Academy of Dermatology Position Statement on Indoor Tanning

- The American Academy of Dermatology Association (AADA) opposes indoor tanning and supports a ban on the production and sale of indoor tanning equipment for nonmedical purposes.
- The American Academy of Dermatology supports the WHO recommendation that minors should not use indoor tanning equipment because indoor tanning devices

<sup>&</sup>lt;sup>20</sup>See, e.g., http://www.fda.gov/Radiation-

EmittingProducts/RadiationEmittingProductsandProcedures/HomeBusinessandEntertainment/ucm116447.htm

<sup>&</sup>lt;sup>21</sup> http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm186687.htm

<sup>&</sup>lt;sup>22</sup> http://www.co.ho.md.us/Health/HealthMain/Health\_HomePage.htm

<sup>&</sup>lt;sup>23</sup> http://www.washingtonwatch.com/bills/show/111\_HR\_4520.html

<sup>&</sup>lt;sup>24</sup> http://thomas.loc.gov/cgi-bin/thomas; http://www.washingtonwatch.com/bills/show/111\_HR\_4520.html

<sup>&</sup>lt;sup>25</sup> http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm186687.htm

<sup>&</sup>lt;sup>26</sup> http://www.ftc.gov/opa/2010/01/tanning.shtm

- emit UVA and UVB radiation, and because overexposure to UV radiation can lead to the development of skin cancer.
- Unless and until the FDA bans the sale and use of indoor tanning equipment for non-medical purposes, the Academy supports restrictions for indoor tanning facilities, including: No person or facility should advertise the use of any UVA or UVB tanning device using wording such as "safe," "safe tanning," "no harmful rays," "no adverse effect," or similar wording or concepts.

#### The American Association of Pediatrics

"All skin damage in childhood, adolescence and young adulthood is a key factor in the development of skin cancer. In fact, most non-melanoma skin cancers (the most common cancer in America) can be attributed to unprotected sun exposure - specifically ultraviolet or "UV-A" and "UV-B" rays...The deadliest form of skin cancer, melanoma, killed about 7,800 people in the United States last year, and that number is expected to rise this year. Melanoma often strikes people who have suffered deep, intense sunburns, particularly in childhood and adolescence. All children under the age of 21 should avoid the use of tanning salons and the Academy supports the efforts to ban the usage in children". 28

## D. The WHO/IARC Report

While concerns about skin cancer and other dangers of tanning have been raised for years by a number of medical authorities, the legislative actions and other actions aimed at potentially restricting or limiting tanning bed usage have increased since the release of a World Health Organization (a WHO) Report in 2006. The Report was conducted by the International Agency for Research on Cancer (IARC). The IARC is the WHO agency that developed the most widely used system for classifying carcinogens. Tanning beds had previously been classified as "probably carcinogenic to humans". A meta-analysis of 19 studies showed an increase risk for all users and a higher risk for those exposed under the age of 35.<sup>29</sup> In response to this report, the WHO and the IARC elevated tanning beds to its highest cancer risk category – "carcinogenic to humans" (Group 1)<sup>30</sup>. (Additional Details on the IARC Report will be found in the health risk section below).

# IV. POTENTIAL OR CLAIMED HEALTH BENEFITS OF TANNING LAMPS OR BEDS

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<sup>&</sup>lt;sup>27</sup> http://www.aad.org/media/background/factsheets/fact\_indoortanning.html

<sup>&</sup>lt;sup>28</sup> Louis Cooper, President of the AAP cited at: <a href="http://www.aap.org/advocacy/releases/safeskin.htm">http://www.aap.org/advocacy/releases/safeskin.htm</a>

<sup>&</sup>lt;sup>29</sup> IARC Working Group on artificial ultraviolet light (UV) and skin cancer: the association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. 2006. Int J. Cancer 120:1116-1122.

<sup>&</sup>lt;sup>30</sup> El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens--part D: radiation. WHO International Agency for Research on Cancer Monograph Working Group. Lancet Oncol. 2009 Aug;10(8):751-2.

Before examining further the potential risks of skin cancers that led to the IARC report and other potential health issues with tanning, are there any health benefits to the use of tanning lamps or beds? There are many commercial sites that promote information stressing potential positive health effects of tanning some of these include: Tan-Tropics – Positive Effects of Tanning on E-how.com<sup>32</sup> and the Optimal Skin Care System – What are Positive Effects of Tanning Beds? <sup>33</sup>

## A. Perceived Cosmetic Benefit

Many people apparently tan because of a perceived cosmetic benefit. Knight and co-investigators in 2002 reported that 92% of college students were aware of the risk of tanning beds but that 47% had reported using a tanning lamp during the last year, because it improved their appearance<sup>34</sup>

# B. A Postulated Reinforcing Physiological "Stimulus" of Tanning Beds

Feldman and co-investigators have suggested that tanning bed usage may have a reinforcing physiological "stimulus" in users. They conducted a small study (N-14) of adults and suggested that tanning bed users report a perception of improved cosmetic benefit. However, 11/14 also chose a UV source light for future tanning over a non-UV light source when the source was blinded. The authors suggest that UV light have a physiologic effect on tanners that reinforces the usage beyond the perceived cosmetic benefit but suggested more research is needed in this area. To date other reviewed literature has not seen or investigated this potential effect.

#### C. Mood or Seasonal Affective Disorder

Investigators have looked at the effect of tanning booths on mood, to fight depression or seasonal affective disorder. The general therapeutic effect of light on seasonal affective disorder (SAD) has been widely acknowledged. However, there is evidence that seasonal affective disorder can be treated by other light therapy devices that do not emit UV radiation and there is no additive benefit from UV radiation. Moreover, the antidepressant effect of light does not seem to be the same for different spectra of light. Lee and co-investigators studied the spectral properties of phototherapy for SAD using a meta-analytical procedure. Their findings suggested that light of short to medium wavelengths (blue/green/yellow) seems to be essential for the therapeutic effect of light on SAD. Red wavelengths were relatively ineffective. It was then postulated that SAD may be

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<sup>&</sup>lt;sup>31</sup> http://www.tantropics.com/positive effects of tanning.htm Accessed on Feb. 15, 2010

http://www.ehow.com/facts 4843414 positive-effects-tanning-beds.html Accessed on Feb 15, 2010

http://www.theita.com/indoor/faq.cfm#ans11 Accessed on 2/15/10

<sup>&</sup>lt;sup>34</sup> Knight JM, Kirincich AN, Farmer ER, Hood AF. Arch Dermatol. Awareness of the risks of tanning lamps does not influence behavior among college students.2002 Oct;138(10):1311-5.

<sup>&</sup>lt;sup>35</sup> Feldman SR, Liguori A, Kucenic M, Rapp SR, Fleischer AB Jr, Lang W, Kaur M. Ultraviolet exposure is a reinforcing stimulus in frequent indoor tanners. J Am Acad Dermatol. 2004 Jul;51(1):45-51.

predisposed and/or precipitated by the inefficiency of the S and M cones in the retina. Furthermore, ultraviolet (UV) waves did not seem to be essential for SAD symptom alleviation by artificial light. These authors reported that, these potentially harmful UV waves should be blocked in any clinical application of phototherapy for SAD.<sup>36</sup> Lam and coworkers found that non-UV light therapy was just as effective as for the treatment of seasonal affective therapy as UV. To assess the clinical effects of UV-A wavelengths (315-400 nm), the authors studied 33 depressed SAD patients diagnosed with structured interviews by DSM-IIIR criteria. Following a baseline week, patients underwent 2 weeks of 2500 lux light therapy for 2 h daily (06:00-08:00). Light therapy consisted of cool-white fluorescent light with the addition of a special UV-A fluorescent tube. Patients were randomized to wear glasses during light therapy that either blocked (UV-blocked condition) or passed (UV-A condition) wavelengths below 400 nm. Both treatments significantly reduced all depression ratings, but no differences were found between the UV-A and UVblocked conditions. The authors concluded that the UV-A spectrum does not increase the antidepressant response of light therapy. Given the potential side effects of chronic UV exposure, clinical application of light therapy should use light sources that have the UV spectrum filtered.<sup>37</sup>

# D. Vitamin D and Tanning Lamps

Within the last several years the health benefits of Vitamin D as a cancer preventive or other health promoting agent have gained proponents, citing potential effects on bone strength, cancer, the immune system and other possible health effects. 38 39 There is also evidence that the U.S population has had decreased intake of Vitamin D or decreased natural production by the sun. Looker and co-investigators have reported a drop in serum Vitamin D levels in the U.S. population in the last two decades of 5-9 ug attributable to decreased intake of Vitamin D and decreased sun exposure comparing results from 289 participants in NHANES 2000-2004 and in 18 158 participants in NHANES III (1988-1994). Devgun et. al showed a moderate rise in Vitamin D levels with tanning, however, the authors concluded this benefit was outweighed by other risks including that of potential melanoma formation. The Edward Giovannucci, a Harvard University professor suggested that his own research showed that vitamin D might help prevent 30 deaths for each one caused by skin cancer. His research on the preventive effect of Vitamin D on the mortality

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<sup>&</sup>lt;sup>36</sup> Lee TM, Chan CC, Paterson JG, Janzen HL, Blashko CA. Lee TM, Chan CC, Paterson JG, Janzen HL, Blashko CA. Spectral properties of phototherapy for seasonal affective disorder: a meta-analysis. <u>Acta Psychiatr Scand.</u> 1997 Aug;96(2):117-21.

<sup>&</sup>lt;sup>37</sup> <u>Lam RW</u>, <u>Buchanan A</u>, <u>Mador JA</u>, <u>Corral MR</u>, <u>Remick RA</u>. The effects of ultraviolet-A wavelengths in light therapy for seasonal depression. <u>J Affect Disord.</u> 1992 Apr;24(4):237-43.

<sup>38</sup> http://www.genovatan.com/residential/health.html

<sup>39</sup> http://www.theita.com/

<sup>&</sup>lt;sup>40</sup> Looker AC, Pfeiffer CM, Lacher DA, Schleicher RL, Picciano MF, Yetley EA. Serum 25-hydroxyvitamin D status of the US population: 1988-1994 compared with 2000-2004. Am J Clin Nutr. 2008 Dec;88(6):1519-27.

<sup>&</sup>lt;sup>41</sup> Devgun MS, Johnson BE, Paterson CR. <u>Tanning, protection against sunburn and vitamin D formation with a UV-A 'sun-bed'</u>. Br J Dermatol. 1982 Sep;107(3):275-84.

<sup>42</sup> http://www.usatoday.com/news/nation/2005-05-21-doctors-sunshine-good\_x.htm

from other cancers (not including melanoma or other cancers) suggested that 1500 ug of Vitamin D may be needed to have a preventive effect but suggested that could be obtained by oral supplementation. Cannell et. al. has stated that there could be situations where the risk benefit of the usage of tanning beds in the prevention of other cancers potentially might outweigh the risk of skin cancer but also stated that the same benefit can be gotten from using dietary supplementation.

The National Cancer Institute (NCI) of the National Institutes of Health (NIH) has issued the their recommendations Vitamin D and UV light exposure from any source: According to NCI: Although people obtain some vitamin D from dietary sources, most vitamin D is made in the body after the skin is exposed to sunlight. Despite the known and potential health benefits of vitamin D, increasing sun exposure increases the risk of skin cancer. In general, most experts believe that people should continue to use sun protection when UV levels are moderate or higher. Some researchers have suggested that brief daily exposure to UV will ensure adequate vitamin D production, but many variables (such as skin color, latitude, and season) can affect the production of vitamin D, and such recommendations have proven controversial. Other experts recommend vitamin D supplementation to avoid the problem of increasing skin cancer risk. <sup>45</sup>

Doctors Woo and Edie, two dermatologists from the Henry Ford Hospital, recently conducted an extensive review of the available literature on Vitamin D and tanning beds and concluded that: Tanning bed proponents cite the health benefits of vitamin D to support indoor tanning, including concerns that reduced vitamin D levels or certain vitamin D receptor polymorphisms may be associated with increased incidence of various cancers, including cutaneous melanoma. However, most tanning devices primarily emit ultraviolet A, which is relatively ineffective in stimulating vitamin D synthesis. Health benefits can be fully dissociated from the ultraviolet exposure risks with vitamin D supplementation, although optimal levels remain to be established. Indoor tanning represents an avoidable risk factor for skin cancer. 46

The WHO has also recently summarized the risk benefit of Vitamin D production from tanning bed and summarized international research on the other purported health or cosmetic benefits:

While sun bed use may increase vitamin D synthesis, predominantly from the UVB component, for the majority of the population, incidental exposure to the sun, combined

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<sup>&</sup>lt;sup>43</sup> Giovannucci E, Liu Y, Rimm EB, Hollis BW, Fuchs CS, Stampfer MJ, Willett WC. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst. 2006 Apr 5:98(7):451-9.

<sup>&</sup>lt;sup>44</sup> <u>Cannell JJ</u>, <u>Hollis BW</u>, <u>Zasloff M</u>, <u>Heaney RP</u>. Diagnosis and treatment of vitamin D deficiency. <u>Expert Opin Pharmacother.</u> 2008 Jan;9(1):107-18

<sup>45</sup> http://www.cancer.gov/cancertopics/factsheet/prevention/vitamin-D

<sup>&</sup>lt;sup>46</sup> Woo DK, Eide MJ. Tanning beds, skin cancer, and vitamin D: an examination of the scientific evidence and public health implications. <u>Dermatol Ther.</u> 2010 Jan;23(1):61-71.

with normal dietary intake of vitamin D, provides adequate vitamin D for a healthy body throughout the year. If people require more vitamin D than the sun can provide (for example, because of living in polar regions) this should be supplemented through diet rather than sunbed use. Aside from tanning, many people claim that use of sun beds helps them to be more relaxed and have a feeling of well being. It is difficult to quantify such claims. Only in very rare and specific cases should the medically-supervised use of sunbeds be considered. Medical UV devices successfully treat certain skin conditions such as dermatitis and psoriasis. These treatments should only be conducted under qualified medical supervision in an approved medical clinic and not unsupervised either in commercial tanning premises or at home using a domestic sunbed. There is also widespread false belief that a tan acquired using a sunbed will offer good skin protection against sunburn for a holiday in a sunny location. In reality, a tan acquired using a sunbed offers only limited protection against sunburn from solar UV. It has been estimated that a sunbed tan offers the same protective effect as using a sunscreen with a sun protection factor (SPF) of only 2-3.<sup>47</sup>

## V. KNOWN OR POSTULATED RISKS OF TANNING LAMPS OR BEDS

A. Summary Effects on Skin, Eyes and other Systems

The WHO has recently provided an overall summary on the risks of tanning lamps and beds: The desire to acquire a tan for fashion or cosmetic purposes has led to a large increase in the use of artificial tanning sunbeds in, mostly, developed countries. Use of sunbeds for tanning continues to increase in popularity, especially among young women.

Sun beds used in solariums, and sun tanning lamps, are artificial tanning devices that claim to offer an effective, quick and harmless alternative to natural sunlight. However, there is growing evidence that the ultraviolet (UV) radiation emitted by the lamps used in solariums may damage the skin and increase the risk of developing skin cancer. Some 132 000 cases of malignant melanoma (the most fatal kind of skin cancer) and over two million cases of other skin cancers occur worldwide each year. One in every three cancers diagnosed worldwide is a skin cancer...Primary among these artificial sources is sunbeds, and a WHO fact sheet describes the known health consequences of tanning bed or sun lamp usage:

 $<sup>^{47}\</sup> http://www.who.int/mediacentre/factsheets/fs287/en/index.html$ 

Exposure to UV, either naturally from the sun or from artificial sources such as sunlamps, is a known risk factor for skin cancer. Short-wavelength UVB (280-315 nm) has been recognized for some time as carcinogenic in experimental animals, and there is increasing evidence that longer-wavelength UVA (315-400 nm) used in sunbeds, which penetrates more deeply into the skin, also contributes to the induction of cancer. Additional exposure to UV from sunbeds is likely to enhance the well-known detrimental consequences of excessive solar UV exposure. There is no evidence to suggest that UV exposure from any type of sunbed is less harmful than UV exposure from the sun. Pre-cancerous actinic keratoses and Bowen's disease have also been found in sunlight-protected but sunbed exposed skin in fair-skinned users after just two to three years of regular sunbed use.

Any excessive exposure to UV, not just from sunbeds, can result in structural damage to human skin. In the short term this damage can be due to burning, fragility and scarring and in the longer-term as photoageing. Photoageing, caused by the breakdown of collagen in the skin by UV, manifests itself as wrinkling and loss of elasticity. The effects of UV on the eye include cataracts, pterygium (a white coloured growth over the cornea) and inflammation of the eye such as photokeratitis and photoconjunctivitis. Furthermore, excessive UV exposure can suppress the immune system, possibly leading to a greater risk of infectious diseases.

Sunbeds emit predominantly UVA and some UVB, both of which can damage the DNA in cells of the skin. However, in recent years, lamps of sunbeds have been manufactured that produce higher levels of UVB to mimic the solar spectrum and speed the tanning process. While UVB has well known carcinogenic properties and whose excessive exposure is known to lead to the development of skin cancers, recent scientific studies suggest that high exposures to the longer wavelength UVA could also have an impact on skin cancer occurrence. As with sun exposure, recent studies indicate a relationship between the use of sunbeds and malignant melanoma as well as non-melanoma skin cancers such as squamous and basal cell carcinomas. Thus, the consequences of regular sunbed use may include disfigurement from removal of skin cancers, early death if the cancer is a malignant melanoma, as well as substantial costs to national health systems for screening, treating and monitoring skin cancer patients. Some skin types are unsuitable for tanning. Based on their susceptibility to sunburn, skin types are classified into six different classes (I - VI). People with skin type I have the lightest skin and may not have even a light tan after repeated exposure to a sunbed. Instead, their skin generally suffers sunburn reactions. People with skin type I are more likely to use sunbeds than people with darker skin. The following table from the Canadian Center for Occupational Health and Safety summarizes the ability to tan vs. burning for various skin types<sup>48</sup>.

<sup>&</sup>lt;sup>48</sup> http://www.ccohs.ca/oshanswers/diseases/skin\_cancer.html

	Classification of Skin Types						
Skin Type	Hair	Complexion	Freckles	Sun Reaction	Tanning		
I	Red or Blond	very fair	+++	always burns	never tans		
II	Blond	fair	++	often burns	tans lightly		
Ш	Blond or Light Brown	fair to medium	+ to 0	sometimes burns	tans progressively		
IV	Brown	Olive	0	rarely burns	tans easily		
V	Brown to Black	dark	0	rarely burns	Tans deeply		
VI	Black	very dark	0	never burns	Tans deeply		

The ability of the consumer to recognize their skin type as not suitable for sunbed use is based on either self-diagnosis, or worst, a bad experience of sunburn...While skin type II and higher can tan, skin damage can still occur following excessive exposure to UV. . . Childhood exposure to UV and the number of times a child is burnt by UV, either from the sun or from sunbeds, are known to increase the risk of developing melanoma later in life. For this reason, particular attention is required to ensure children and adolescents do not use sunbeds. The United States Department of Health and Human Services has classified exposure to sunlamps or sunbeds as "known to be carcinogenic to humans" and states that the longer the exposure, the greater the risk, especially to people exposed before the age of 30 years.

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a malignant melanoma, as well as substantial costs to national health systems for screening, treating and monitoring skin cancer patients.<sup>49</sup>

#### B. The Risk of Burns

This review could find no published literature specifically on the risk of burns from tanning beds and currently as tanning beds are a class I device under-reporting of burns may be occurring (attached to this summary is a review of reported burns from tanning beds to the FDA). However, as noted earlier Cokkinides and co-investigators in a survey of tanning bed usage in adolescents from 1998-2004 reported that in two serials population based surveys (N=1196) and 2004 (N=1613), 58% of the total respondents reported some type of burns due to tanning in the last year. The last year of the total respondents reported some type of burns due to tanning in the last year. It is probable that many of these burns are mild but also indicate that the total radiation level of exposure in order to try to produce a tan rapidly in many teenagers (and probably) in adults is also causing other skin damage as well as a under-reporting of burns to the FDA and other medical authorities. (There have been a small number of burns and injuries reported to the FDA during the last decade but with the device being currently a Class I device it is thought these burns are under-reported — please see the SAER Report in the appendix for details on these injuries potentially attributed to tanning bed or lamp usage.)

#### C. The Risk of Skin Cancers

Most of the theoretical healths concern raised with the usage of tanning beds or lamps is on the potential for cancer development. It is known that ionizing radiation, transfers energy in the form of highly structured tracks of ionisation and excitation events that can produce a variety of molecular lesions and clustered, complex DNA damage. Subsequent processing of this damage induces many responses (e.g., cell killing, chromosomal aberrations, mutations, genomic instability, cell transformation, and bystander effects) that contribute to carcinogenesis. Based on these mechanistic considerations, all types of UV radiation were classified by the IARC Working Group as "carcinogenic to humans" (Group 1). This summary will discuss the various types of skin cancers thought to be at increased risk from UV

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<sup>&</sup>lt;sup>49</sup> <a href="http://www.who.int/mediacentre/factsheets/fs287/en/index.html">http://www.who.int/mediacentre/factsheets/fs287/en/index.html</a> [According to the site: Information for this fact sheet comes from WHO sponsored meetings and workshops, recent scientific literature, reviews by WHO Member States and the recommendations of international NGOs. ]

<sup>&</sup>lt;sup>50</sup> Cokkinides V, Weinstock M, Lazovich D, Ward E, Thun M. Indoor tanning use among adolescents in the US, 1998 to 2004. Cancer. 2009 Jan 1;115(1):190-8.

<sup>&</sup>lt;sup>51</sup> Goodhead DT. Initial events in the cellular effects of ionizing radiations: clustered damage in DNA. *Int J Radiat Biol* 1994; 65: 7-17.

radiation, with an emphasis on that of melanoma, the most widely studied cancer that is potentially associated with tanning bed usage. 52

#### 1. SCC or BCC Carcinomas.

Karagus and her co-authors from Dartmouth Medical School reported in 2002 that they had conducted a population-based, case-control study that included 603 basal cell carcinoma (BCC) case patients, 293 squamous cell carcinoma (SCC) case patients, and 540 control subjects. Study participants were interviewed in person to obtain information on tanning device use, sun exposure history, sun sensitivity, and other risk factors for skin cancer. Overall, any use of tanning devices was associated with odds ratios of 2.5 (95% confidence interval [CI] = 1.7 to 3.8) for SCC and 1.5 (95% CI = 1.1 to 2.1) for BCC. Adjustment for history of sunburns, sunbathing, and sun exposure did not affect the results. 53

Other studies, primarily of the case control type and/or case series type, have suggested, but not definitely proven, a potential link between tanning bed usage and either basal cell carcinoma and squamous cell usage. 54 55 56

The 2006 IARC Report mentioned above performed a meta-analysis on 5 studies including the one cited above by Karagus and demonstrated the following:

The meta-analysis was based on the 5 studies cited by the IARC (see attached paper) reporting type-specific risk estimates. Meta analytic estimates suggested a significant effect of exposure to indoor tanning appliances for SCC, but not for BCC. Funnel plot regression gave no indication of publication bias (p = 0.26 and 0.77 for SCC and BCC, respectively). . . Depending on age at first use, the risks for BCC and SCC were found to increase by 10% (OR, 1.1; CI, 0.9-1.5) and 20% (OR, 1.2; CI, 0.) The results from the IARC suggest a possible link between the use of tanning beds and non-melanomas skin cancers, although the OR are not dramatic and overlap unity.  $^{57}$ 

#### 2. Melanoma

<sup>&</sup>lt;sup>52</sup> El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V. A review of human carcinogens--part D: radiation. WHO International Agency for Research on Cancer Monograph Working Group. Lancet Oncol. 2009 Aug;10(8):751-2.

<sup>&</sup>lt;sup>53</sup> <u>Karagas MR</u>, <u>Stannard VA</u>, <u>Mott LA</u>, <u>Slattery MJ</u>, <u>Spencer SK</u>, <u>Weinstock MA</u>. Use of tanning devices and risk of basal cell and squamous cell skin cancers. <u>J Natl Cancer Inst.</u> 2002 Feb 6;94(3):224-6

<sup>&</sup>lt;sup>54</sup> Boyd AS, Shyr Y, King LE Jr. Basal cell carcinoma in young women: an evaluation of the association of tanning bed use and smoking. J Am Acad Dermatol. 2002 May;46(5):706-9.

<sup>&</sup>lt;sup>55</sup> Lever LR, Lawrence CM. Nonmelanoma skin cancer associated with use of a tanning bed. N Engl J Med. 1995 May 25;332(21):1450-1.

<sup>&</sup>lt;sup>56</sup> Geller AC, Brooks DR, Colditz GA, Koh HK, Frazier AL. Sun protection practices among offspring of women with personal or family history of skin cancer. Pediatrics. 2006 Apr;117(4):e688-94.

<sup>&</sup>lt;sup>57</sup> IARC Working Group on artificial ultraviolet light (UV) and skin cancer: the association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. 2006. Int J. Cancer 120:1116-1122.

There are more reviews of the risk of melanoma published in the peer-reviewed literature than for other skin cancers, some frequently cited reviews or studies include:

Gallagher and his co-workers did a meta-analysis of the risk of melanoma, with the usage of tanning bed and sun lamps in 2005. They reported that they did a review of the literature from Jan 1, 1984 to April 2004 and identified 12 case-control studies and 1 cohort study which quantitatively evaluated the use of sunlamps and/or sun beds and subsequent melanoma. After applying exclusion/inclusion criteria, 9 case-control and 1 cohort study provided data for the analysis. Ten studies provided data for assessment of melanoma risk among subjects who reported "ever" being exposed compared with those "never" exposed. A positive association was found between exposure and risk (summary OR, 1.25; 95% CI, 1.05-1.49). Significant heterogeneity between studies was present. Evaluation of the metrics "first exposure as a young adult" (5 studies) and "longest duration or highest frequency of exposure" (6 studies) also yielded significantly elevated risk estimates (summary OR, 1.69; 95% CI, 1.32-2.18, and 1.61; 95% CI, 1.21-2.12, respectively, with no heterogeneity in either analysis). They concluded that there was a significantly increased risk of cutaneous melanoma subsequent to sun bed/sunlamp exposure. <sup>58</sup>

Westerdahl and his co-workers reported on their case control study using more than 400 melanoma patients in Sweden in 1994 whereby they showed a positive association for developing malignant melanoma after ever having used sun beds or sunlamps of 1.3. This odds ratio was significantly elevated after exposure more than 10 times a year to sun beds or sunlamps (odds ratio (OR) = 1.8) suggesting to the authors a fairly strong dose response relationship.  $^{59}$ 

Dore' and his co-workers conducted a large European case control study and reported that exposure to sunlamps or sun beds at least a decade before was associated with a crude estimated risk of CMM of 2.71 (95% CI: 1.06-7.78) for at least 10 hr of accumulated exposure.<sup>60</sup>

Han and his co-workers conducted a nested case control study using data from the national Women's Health study in 2006 and reported that sunlamp usage or tanning salon

Gallagher RP, Spinelli JJ, Lee TK, Tanning beds, sunlamps, and risk of cutaneous malignant melanoma.
 Cancer Epidemiol Biomarkers Prev. 2005 Mar;14(3):562-6.
 Westerdahl J, Olsson H, Måsbäck A, Ingvar C, Jonsson N, Brandt L, Jönsson PE, Möller T. Use of sunbeds

westerdahl J, Olsson H, Måsbäck A, Ingvar C, Jonsson N, Brandt L, Jönsson PE, Möller T. Use of sunbeds or sunlamps and malignant melanoma in southern Sweden. Am J Epidemiol. 1994 Oct 15;140(8):691-9.

Mattier P, Doré JF, Lejeune F, Koelmel KF, Geffeler O, Hille P, Cesarini JP, Lienard D, Liabeuf A, Joarlette M, et al. Cutaneous malignant melanoma and exposure to sunlamps or sunbeds: an EORTC multicenter case-control study in Belgium, France and Germany. EORTC Melanoma Cooperative Group. Int J Cancer. 1994 Sep 15:58(6):809-13.

attendance was a fairly strong risk factor for melanoma after adjusting for potential confounding variables (OR for ever vs never usage, 2.06, 95% CI 1.30-3.26). <sup>61</sup>

Ting and his co-workers reported that there was a strong association for a recall of tanning bed usage in women who had skin cancers, and in particular, for melanoma in patients surveyed in academic dermatology clinics. Of 1518 patients surveyed, 487 (32.1%) reported tanning bed exposure. Women aged 45 years or younger accounted for about 60% of all tanning bed users. Seventy-nine cases of malignant melanoma were reported, 22 in women aged 45 years or younger. In the entire cohort, the "ever-use" of tanning beds was found to be a significant risk factor for the development of melanoma [P < 0.05; odds ratio (OR), 1.64; 95% confidence interval (95% CI), 1.01-2.67]. The risk was greater in women aged 45 years or younger (P < 0.05; OR, 3.22; 95% CI, 1.01-11.46). Patients with a history of melanoma were significantly more likely to report tanning bed sessions exceeding 20 min (P < 0.01; OR, 3.18; 95% CI, 1.48-6.82); this association was even stronger for women aged 45 years or younger (OR, 4.12; 95% CI, 1.41-12.02). The authors concluded that the study was subject to recall bias but stated that this was consistent with a hypothesis that exposure to tanning beds increases the risk of malignant melanoma, especially in women aged 45 years or younger.

Clough-Gorr and co-workers reported in 2008 on a case control study in New Hampshire on a modest association between tanning lamp usage and a confirmed diagnosis of melanoma (OR was 1.14 (95% CI 0.80-1.61) for ever using a tanning bed) that is close to that seen in the IARC report (see below) and their data also suggested increasing risk with number of sunlamp uses and with duration of use (tests of trend p = 0.02).

In 2008 Marianne Berwick, PhD, of the University of New Mexico reviewed the available literature on the risk of melanoma and concluded that the data suggest, but do not prove, that tanning beds are no safer than sun exposure and may even be associated with an increased risk for melanoma. She stated that although better studies are needed to investigate the issue, adding that, "because of this uncertainty, the data do not support a claim that sun beds are safe, and such claims should be considered misleading." <sup>64</sup>

The 2006 IARC Report was a meta-analysis using 23 studies on the use of indoor tanning equipment and melanoma and provided additional evidence that there is a probable increased risk of melanoma due to the use of tanning beds. In the analysis a total of four of the identified studies were excluded from the meta-analysis because they did not include

<sup>&</sup>lt;sup>61</sup> <u>Han J, Colditz GA, Hunter DJ</u>. <u>Int J Epidemiol</u>. Risk factors for skin cancers: a nested case-control study within the Nurses' Health Study. 2006 Dec;35(6):1514-21. Epub 2006 Aug 30.

<sup>&</sup>lt;sup>62</sup> <u>Ting W</u>, <u>Schultz K</u>, <u>Cac NN</u>, <u>Peterson M</u>, <u>Walling HW</u>. Tanning bed exposure increases the risk of malignant melanoma. <u>Int J Dermatol.</u> 2007 Dec;46(12):1253-7.

<sup>&</sup>lt;sup>63</sup> Clough-Gorr KM, <u>Titus-Ernstoff L</u>, <u>Perry AE</u>, <u>Spencer SK</u>, <u>Ernstoff MS</u>. Exposure to sunlamps, tanning beds, and melanoma risk. <u>Cancer Causes Control.</u> 2008 Sep;19(7):659-69. Epub 2008 Feb 14.

<sup>&</sup>lt;sup>64</sup> Berwick M. Are tanning beds "safe"? Human studies of melanoma. Pigment Cell Melanoma Res. 21;517-519.

estimates of the relative risk for cutaneous melanoma associated with exposure to tanning appliances. The studies used were published in 1981 and the last in 2005. Of the 19 studies included in the meta-analysis, thirteen studies had positive results (for ever versus never exposed) to indoor tanning equipment for melanoma, with four 4 of these reaching statistical significance.

The risk of melanoma from the use of indoor tanning equipment was estimated by the IARC's analysis as provided in the following table:

## **Indoor Tanning and Melanoma Risk**

Exposure	Number of Studies	Relative Risk for Melanoma
Ever use	19	1.15 (1.00 -1.31)
First exposure in youth	7	1.75 (1.35 -2.26)
Exposure distant in time	e 5	1.49 (0.93 -2.38)
Exposure recent in time	5	1.10 (0.76 – 1.60)

To decrease the influence of possible biases, additional estimates were calculated including only the cohort and the 9 population-based case-control studies. The summary relative risk was very similar apart from having wider Cls (RR, 1.17; Cl, 0.96-1.42). Four studies looked at a potential dosage relationship: There was some indication for a dose-effect relationship in 2 studies, but not in the other two.

The IARC's systematic review of published studies mainly from Europe and North America of the association of use of indoor tanning equipment, including UV lamps for tanning, with skin cancers revealed an association of age at first use of less than 35 years with melanoma risk. According to the authors these studies consistently indicated a moderate strength of association, with a summary relative risk of 1.75 (1.35-2.26). To the authors these results suggest a greater vulnerability of younger people to the carcinogenic impact of indoor tanning and are in agreement with the knowledge that age at exposure may influence the relative risk for skin cancer associated with UV exposure.

The association with ever using such equipment, or use more than 15-20 years prior to diagnosis of melanoma, was weak, and evidence regarding a dose-response relationship was scant. The evidence is limited by concerns over characterization of exposure and recall of exposure by individuals, potential confounding by sun exposure or other variables and the low power to detect associations that become evident only following a prolonged lag period after exposure.

On balance, the authors stated that the evidence pertaining to the strength, consistency, dose-response and temporal sequence of the association of the use of indoor tanning equipment with melanoma risk, and of the coherence and biologic plausibility of the

association, leads us to conclude that there is convincing evidence to support a causal relationship, particularly with exposure before the age of 35 years. This evidence was to the IARC strongly suggestive. They did state that "further studies could clarify our understanding of this association and allow more definitive conclusions". <sup>65</sup>

The primary theoretical issue with this report is that most of the studies were case control studies. Case control studies while they are valuable to study possible associations between rare diseases and risk factors are subject to confounding and biases, especially that of recall biases and the ability to ascertain the exposure accurately. Such measurement and biases are common in studies of melanoma risk. <sup>66</sup> The authors did a meta-analysis on the remaining 7 cohort studies and found a similar 1.17:1 RR vs. the 1.15:1 RR for overall exposure for all ages.

The major conclusion the IARC Report is the moderate RR of 1.75:1 for exposure under the age of 35. While this is suggestive of a weak to moderate association there were several issues with this potential association: 1) the authors do not describe how they arrived at looking at risk below the age of 35 vs. other possible age stratifications; 2) as was noted above, most of the studies were case control and subject to recall and exposure ascertainment biases; and 3) there was a nonsignificant test of heterogeneity studies used, i.e., p = 0.55, potentially limiting the ability to draw conclusions across the studies.

Do to a paucity of studies and the lack of the ability to retroactively accurately estimate dosage received in many studies, the IARC report did not document a dose response relationship which if it had been demonstrated, would have provided additional evidence for the association. Another potential issue with this review and most others is that they do not break down the skin cancer risk by skin types potentially most at risk for tanning behavior.

Nevertheless, the IARC Report does add to a body of literature suggesting that there may be a small to moderate risk of skin cancer, independently due to the use of tanning beds or lamps - with the majority of studies concentrating on the risk of melanoma. Moreover, this association may be stronger with the usage of tanning beds or lamps in children consistent with the postulated increased dangers of melanoma in children or young adults due to sunburns or other UV exposure. <sup>67</sup>

#### VI. CONCLUSION

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<sup>&</sup>lt;sup>65</sup> IARC Working Group on artificial ultraviolet light (UV) and skin cancer: the association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. 2006. Int J. Cancer 120:1116-1122.

<sup>&</sup>lt;sup>66</sup> Parr CL, Hjartåker A, Laake P, Lund E, Veierød MB. <u>Recall bias in melanoma risk factors and measurement error effects: a nested case-control study within the Norwegian Women and Cancer Study.</u> Am J Epidemiol. 2009 Feb 1;169(3):257-66. Epub 2008 Nov 14.

<sup>&</sup>lt;sup>67</sup> <u>Harrison SL</u>, <u>MacLennan R</u>, <u>Buettner PG</u>. Sun exposure and the incidence of melanocytic nevi in young Australian children. <u>Cancer Epidemiol Biomarkers Prev.</u> 2008 Sep;17(9):2318-24

As discussed in this Executive Summary, FDA is aware of potential increased risk for skin cancer associated with increased UV exposure such as that achievable with exposure to UV lamps for indoor tanning. No adequate evidence have been submitted to FDA by tanning bed manufacturers in support of any potential health benefits, not potentially achievable by safer means, for indoor tanning lamps to allow for revision of labeling for these device products. Various governmental and non-governmental health care agencies have recommended that the known risks outweigh any potential for benefit for these device products when used for indoor tanning.

Currently UV lamps for tanning are regulated by FDA (using its regulatory paradigm where Class I is considered low risk and Class III as highest risk) as Class I exempt devices. Current regulations for these devices are in the process of being revised. Consideration is also being given to reclassification of these devices. The Panel is asked to answer a series of questions related to the usage of tanning lamps to advise the agency on future regulatory action